

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims**

Claims 1-19 (canceled)

Claim 20 (new): A method for diagnosis of an inflammatory, a fibrotic or a cancerous disease in a patient comprising the steps of:

- a) measuring the values of biochemical markers in the serum or plasma of said patient;
- b) combining said values through a logistic function including said markers; and
- c) analyzing the end value of said logistic function in order to determine the presence of liver fibrosis and/or liver necroinflammatory lesions in said patient.

Claim 21 (new): The method of claim 20, wherein the logistic function is obtained through the following method:

- a) classification of the patients in different groups according to the extent of their disease;
- b) identification of factors which differ significantly between these groups by unidimensional analysis;
- c) logistic regression analysis to assess the independent discriminative value of markers for the diagnosis of fibrosis and/or liver necroinflammatory lesions; and

- d) construction of the logistic function by combination of these identified independent factors.

Claim 22 (new): The method of claim 20, wherein at least 4 biochemical markers are studied in step a).

Claim 23 (new): The method of claim 20, wherein said markers are selected from the group consisting of  $\alpha$ 2-macroglobulin, AST, ALT, GGT,  $\gamma$ -globulin, total bilirubin, albumin,  $\alpha$ -globulin,  $\alpha$ 2-globulin, haptoglobin,  $\beta$ -globulin, apoA1, IL10, TGF- $\beta$ 1, apoA2, apo $\beta$ .

Claim 24 (new): The method of claim 20, wherein the logistic function further takes the age and gender of the patient into account.

Claim 25 (new): The method of claim 20, wherein said measured biochemical markers used for diagnosis of fibrosis include  $\alpha$ 2-macroglobulin, GGT,  $\gamma$ -globulin, total bilirubin, ( $\alpha$ 2-globulin or haptoglobin) and apoA1.

Claim 26 (new): The method of claim 20, wherein said measured biochemical markers used for diagnosis of presence of necroinflammatory lesions include  $\alpha$ 2-macroglobulin, GGT,  $\gamma$ -globulin, (ALT or AST) and apoA1.

Claim 27 (new): The method of claim 20, wherein the logistic function is selected from the group consisting of:

$$\begin{aligned} -f_1 = & a_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - a_2 \times [\alpha 2\text{-globulin (g/l)}] + a_3 \times \text{Log} [\text{GGT} \\ & (\text{IU/l})] + a_4 \times [\gamma\text{-globulin (g/l)}] + a_5 \times [\text{Age (years)}] + a_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - a_7 \\ & \times [\text{ApoA1 (g/l)}] + a_8 \times [\text{Sex (female=0, male=1)}] - a_9, \text{ with} \\ & - a_1 \text{ comprised between 6.5 and 6.9,} \end{aligned}$$

- $a_2$  comprised between 0.450 and 0.485,
- $a_3$  comprised between 1.100 and 1.300,
- $a_4$  comprised between 0.0700 and 0.0750,
- $a_5$  comprised between 0.0265 and 0.0300,
- $a_6$  comprised between 1.400 and 1.700,
- $a_7$  comprised between 0.900 and 1,
- $a_8$  comprised between 0.300 and 0.450, and
- $a_9$  comprised between 4.200 and 4.700.

-  $f_2 = b_1 \times \text{Log} [\alpha_2\text{-macroglobulin (g/l)}] - b_2 \times [\alpha_2\text{-globulin (g/l)}] + b_3 \times \text{Log} [\text{GGT (IU/l)}] + b_4 \times [\gamma\text{-globulin (g/l)}] + b_5 \times [\text{Age (years)}] + b_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - b_7 \times [\text{ApoA1 (g/l)}] + b_8 \times [\text{Sex (female=0, male=1)}] + b_9 [\text{Albumin (g/l)}] + b_{10} [\alpha_1\text{-globulin (g/l)}] - b_{11} [\beta_2\text{-globulin (g/l)}] 2.189 - b_{12} \times \text{Log} [\text{ALT (IU/l)}] - b_{13}$ , with

- $b_1$  comprised between 9.9 and 10.2,
- $b_2$  comprised between 0.7 and 0.77,
- $b_3$  comprised between 2 and 2.4,
- $b_4$  comprised between 0.1 and 0.2,
- $b_5$  comprised between 0.04 and 0.07,
- $b_6$  comprised between 4 and 4.6,
- $b_7$  comprised between 2 and 2.5,
- $b_8$  comprised between 0.28 and 0.32,
- $b_9$  comprised between 0.025 and 0.04,

- $b_{10}$  comprised between 2 and 2.2,
- $b_{11}$  comprised between 0.1 and 0.16,
- $b_{12}$  comprised between 0.7 and 0.9, and
- $b_{13}$  comprised between 12 and 14.

-  $f3 = c_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - c_2 \times [\beta 2\text{-globulin (g/l)}] + c_3 \times \text{Log} [\text{GGT (IU/l)}] + c_4 \times [\gamma\text{-globulin (g/l)}] - c_5 \times [\text{Age (years)}] + c_6 \times \text{Log} [\text{ALT (IU/l)}] - c_7 \times [\text{ApoA1 (g/l)}] - c_8 \times [\text{Sex (female=0, male=1)}] - c_9$ , with

- $c_1$  comprised between 3.45 and 3.65,
- $c_2$  comprised between 0.3 and 0.4,
- $c_3$  comprised between 0.8 and 1,
- $c_4$  comprised between 0.075 and 0.09,
- $c_5$  comprised between 0.0015 and 0.003,
- $c_6$  comprised between 2.1 and 2.5,
- $c_7$  comprised between 1.55 and 1.75,
- $c_8$  comprised between 0.35 and 0.45, and
- $c_9$  comprised between 4 and 4.6.

-  $f4 = d_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - d_2 \times [\alpha 2\text{-globulin (g/l)}] + d_3 \times \text{Log} [\text{GGT (IU/l)}] + d_4 \times [\gamma\text{-globulin (g/l)}] + d_5 \times [\text{Age (years)}] + d_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - d_7 \times [\text{ApoA1 (g/l)}] + d_8 \times [\text{Sex (female=0, male=1)}] + d_9 \times \text{Log} [\text{ALT (IU/l)}] - d_{10}$ , with

- $d_1$  comprised between 5.3 and 6.7,
- $d_2$  comprised between 0.45 and 0.5,

- d<sub>3</sub> comprised between 0.8 and 1.2,
- d<sub>4</sub> comprised between 0.06 and 0.08,
- d<sub>5</sub> comprised between 0.0015 and 0.0025,
- d<sub>6</sub> comprised between 1 and 1.2,
- d<sub>7</sub> comprised between 1 and 1.2,
- d<sub>8</sub> comprised between 0.09 and 1.1,
- d<sub>9</sub> comprised between 1.2 and 1.5, and
- d<sub>10</sub> comprised between 4 and 5.

- f5 = z<sub>1</sub> x Log [ $\alpha$ 2-macroglobulin (g/l)] – z<sub>2</sub> x Log [Haptoglobin (g/l)] + z<sub>3</sub> x Log [GGT (IU/l)] + z<sub>4</sub> x [Age (in years)] + z<sub>5</sub> x Log [Bilirubin (umol/l)] – z<sub>6</sub> x [ApoA1 (g/l)] + z<sub>7</sub> x Sex (female=0, male=1) – z<sub>8</sub>, with

- z<sub>1</sub> comprised between 4 and 5,
- z<sub>2</sub> comprised between 1.2 and 1.5,
- z<sub>3</sub> comprised between 0.9 and 1.1,
- z<sub>4</sub> comprised between 0.0026 and 0.03,
- z<sub>5</sub> comprised between 1.6 and 1.9,
- z<sub>6</sub> comprised between 1 and 1.3,
- z<sub>7</sub> comprised between 0.25 and 0.35, and
- z<sub>8</sub> comprised between 5 and 6.

Claim 28 (new): The method of claim 27, wherein the logistic function is selected from the group consisting of:

- fl-a = 6.826 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 0.479 x [ $\alpha$ 2-globulin (g/l)] + 1.252 x Log [GGT (IU/l)] + 0.0707 x [ $\gamma$ -globulin (g/l)] + 0.0273 x [Age (years)] + 1.628 x Log [Bilirubin (umol/l)] - 0.925 x [ApoA1 (g/l)] + 0.344 x [Sex (female=0, male=1)] - 4.544.

- fl-b = 6.552 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 0.458 x [ $\alpha$ 2-globulin (g/l)] + 1.113 x Log [GGT (IU/l)] + 0.0740 x [ $\gamma$ -globulin (g/l)] + 0.0295 x [Age (years)] + 1.473 x Log [Bilirubin (umol/l)] - 0.979 x [ApoA1(g/l)] + 0.414 x [Sex (female=0, male=1)] - 4.305.

- f2 = 10.088 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 0.735 x [ $\alpha$ 2-globulin (g/l)] + 2.189 x Log [GGT (IU/l)] + 0.137 x [ $\gamma$ -globulin (g/l)] + 0.0546 x [Age (years)] + 4.301 x Log [Bilirubin (umol/l)] - 2.284 x [ApoA1 (g/l)] + 0.294 x [Sex (female=0, male=1)] + 0.0312 [Albumin (g/l)] + 2.109 [ $\alpha$ 1-globulin (g/l)] - 0.136 [ $\beta$ 2-globulin (g/l)] - 0.813 x Log [ALT (IU/l)] - 13.165.

- f3 = 3.513 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 0.354 x [ $\beta$ 2-globulin (g/l) (g/l)] + 0.889 x Log [GGT (IU/l)] + 0.0827 x [ $\gamma$  -globulin (g/l)] - 0.0022 x [Age (years)] + 2.295 x Log [ALT (IU/l)] - 1.670 x [ApoA1 (g/l)] - 0.415 x [Sex (female=0, male=1)] - 4.311.

- f4 = 5.981 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 0.481 x [ $\alpha$ 2-globulin (g/l)] + 0.965 x Log [GGT (IU/l)] + 0.0679 x [ $\gamma$ -globulin (g/l)] + 0.0190 x [Age (years)] + 1.143 x Log [Bilirubin (umol/l)] - 1.097 x [ApoA1 (g/l)] + 0.092 x [Sex (female=0, male=1)] + 1.355 Log [ALT (IU/l)] - 4.498.

- f5 = 4.467 x Log [ $\alpha$ 2-macroglobulin (g/l)] - 1.357 x Log [Haptoglobin (g/l)] + 1.017 x Log [GGT (IU/l)] + 0.0281 x [Age (in years)] + 1.737 x Log [Bilirubin (umol/l)] - 1.184 x [ApoA1 (g/l)] + 0.301 x Sex (female=0, male= 1) - 5.540.

Claim 29 (new) The method of claim 20, wherein the end value of the logistic function is used for the diagnosis of cirrhosis.

Claim 30 (new) The method of claim 20, wherein the end value of the logistic function is used to predict the evolution of the disease.

Claim 31 (new) The method of claim 20, wherein the end value of the logistic function is used for the choice of a suitable treatment for the patient.

Claim 32 (new) The method of claim 20, wherein the end value of the logistic function is used in the decision of performing a liver biopsy on said patient.

Claim 33 (new) The method of claim 20, wherein said patient suffers from a disease involving liver fibrosis, optionally developing to cirrhosis.

Claim 34 (new) The method of claim 33, wherein said disease is included in the group consisting of hepatitis B and C, alcoholism, hemochromatosis, metabolic disease, diabetes, obesity, autoimmune liver disease, primary biliary cirrhosis,  $\alpha$ 1-antitrypsin deficit, and Wilson disease.

Claim 35 (new) The method of claim 33, wherein said disease is hepatitis C virus infection.

Claim 36 (new) Kit of diagnosis of an inflammatory, a fibrotic or a cancerous disease, in a patient, comprising instructions allowing to determine the presence of said inflammatory, fibrotic or cancerous disease in said patient, after the dosage of biochemical markers.